REMARKS

The present paper is presented in response to the office action dated July 22, 2010. This paper is being filed with a petition and fee for a two-month extension of time to respond and as such, the response is timely filed on December 22, 2010. This response is accompanied by a Notice of Appeal.

A. Status of the Claims

Claims 21, 22, 24-26, and 32-37 were pending in the instant application. Claim 32 was rejected for failing to comply with the written description requirement. Claims 21, 24 and 26 were rejected under was rejected under 35 U.S.C. 102(b) based on the disclosure of WO 92/21375 and claims 21, 24-25 and 26 were rejected under 35 U.S.C. 103 over a combination of WO 92/21375 and Moorman et al (J. Virology, vol 70, pages 763-770) and also in view of Drew et al.

B. Brief Description of the Subject Matter of Claims as Amended

In the amendment present above, Applicants have ensured that each of the claims recites a DNA sequence that encodes an infectious RNA virus. There are no claims directed to an isolated virus or an RNA sequence. The present application describes that the problem with plus strand RNA viruses is that: these viruses do not encompass a DNA step in their replication and as such in recombinant technologies, infectious clones i.e. ,a DNA copy have to be developed before recombinant DNA techniques can be applied to generate the modified viruses. However, prior to the present invention these infectious clones were not generated because it was not known that the 5' end of the genome (in the

present claims the sequence of SEQ ID NO:18) was not known and this is a critical part of producing the infectious DNA sequence.

C. Rejection under 35 U.S.C. 112, first paragraph

Claim 32 was rejected for lack of written description under 35 U.S.C. §112, first paragraph. In the rejection, the Examiner noted that Claim 32 requires a full length infectious clone that expresses a heterologous Orf7 whereas Paragraph 18 of the specification describes a chimera that consists of a replaced Orf7. Applicants have previously amended claim 32 to insert the term "wherein the chimeric virus expresses the ORF 7 of PRSS strain ATCC VR2332_instead of the ORF 7 of PRSS strain CNCM I-1102". Applicants believe that the claim as presented is fully described at Paragraph 18 which place in the specification expressly states:

> "Such modifications are, for instance, provided by the **PRRSV infectious clones in which** the nucleic acid sequence encoding the **ORF7 N protein is replaced by the ORF7 protein of ATCC VR2332** or LDV"

Nevertheless, the Examiner maintained the rejection. In maintaining the rejection, the Examiner recites to the case law and states:

> "applicants teaching does not commensurate with the scope of patent protection. Applicants were not in possession of the construct claimed and the specification does not teach how to make it. The disclosure does not possess what it claims. The specification does not set forth the metes and bounds of that encompass, and there is not enough information about it in the literature either to guide the one of ordinary skill in the art to predict the

undisclosed regions where the region may encompass. Thus the disclosure fails to provide a meaningful disclosure and possession of the scope of the now claimed invention"

Applicants respectfully traverse this rejection and request a review and consideration of the rejection. Initially, Applicants request clarification of the above-recited paragraph as while it appears to be articulating that the Applicants are rejected for lack of written description and possession of the invention, the applicants cannot ascertain what the Examiner believes is lacking from the specification.

The specification shows that PRRS virus strain 2332 was deposited with ATCC at the time the application was filed (see description in published specification paragraph 008 which refers to ATCC VR2332). The specification at the same location teaches that PRRS virus has been sequenced and contains "six structural proteins of which four envelope glycoproteins named GP2 (ORF2), GP3 (ORF3), GP4 (ORF4) and GP5 (ORF5), a non-glycosylated membrane protein M (ORF6) and the nucleocapsid protein N (ORF7) (Meulenberg et al. 1995, 1996; van Nieuwstadt et al., 1996)." (published specification paragraph 008). Thus, at the time the instant specification was filed PRRS 2332 was available to the person of skill in the art, the sequence of ORF7 was annotated and hence was known to those skilled in the art. Given that the present application teaches the person skilled in the art to make "**PRRSV infectious clones in which** the nucleic acid sequence encoding the **ORF7 N protein is replaced by the ORF7 protein of ATCC VR2332**" Applicants submit that claim 32 is full described in the specification in a manner that shows constructive possession of the invention. In

addition, Paragraph 0070 of the published application expressly teaches that the "genome-length infectious clone was used to generate a chimeric virus expressing the nucleocapsid protein of PRRSV strain ATCC VR2332". Thus at the time the application was filed the Applicants had actual possession of such a chimeric virus.

Applicants thus respectfully request that the Examiner withdraw the rejection with respect to claim 32.

D. Rejection under 35 U.S.C. 102(b)

Claims 21, 24 and 26 were rejected under 35 U.S.C. 102(b) as anticipated by WO 92/21375. As noted above is section B the claims of the present invention relate to **an isolated DNA sequence** that encodes an infectious virus and that is capable of infecting cells that are not permissive to infection by PRRS virus. This is an important distinction as prior to the invention it was not possible to generate full length **DNA clones of PRRS virus which is an RNA virus.** The distinction between DNA clones and RNA viruses appears to have been ignored in the rejection and Applicants respectfully request reconsideration of this rejection. Moreover, claim 21, from which the remaining claims depend expressly recites that the DNA sequence comprises SEQ ID NO:18 at its 5' end. The Wensvoort et al reference WO 92/21375 fails to teach such a DNA sequence having SEQ ID NO:18 at its 5' end. While the WO 92/21375 provides a basic disclosure of the nucleic acid sequence of the RNA virus, the 5' sequence of SEQ ID NO:18 is not shown in WO 92/21375. That document states that:

> The nucleotide sequence of the genomic RNA of LV was determined from overlapping cDNA clones. A consecutive sequence of 15,088 bp was obtained covering nearly the complete genome of LV (Fig. 1). In this sequence 8 open reading frames (ORFs) were identified: ORF 1A, ORF 1B, and ORFs 2 to 7.

Importantly, however, the sequence of SEQ ID NO:18 (ATGATGTGTAGGG), which resides at the 5' end of the virus was not described in WO 92/21375. The Examiner notes that the sequence of SEQ ID NO:18 is an inherent feature of the PRRS virus known as CNCMI-1102. Regardless of whether the PRRS isolate of CNCMI-1102 contains a sequence of SEQ ID NO:18 or not, the skilled person reviewing the disclosure of WO 92/21375 would not have been able to prepare an infectious DNA clone absent some additional guidance which is not present in either WO 92/21375 or any other art cited by the Examiner. As such, the WO92/21375 reference cannot be used under 35 U.S.C. 102(b) for subject matter that describes a DNA sequence that produces an infectious clone. As such, the rejection of claims 21, 24 and 26 under 102(b) in view of Wenswoort et al should be withdrawn.

E. Rejection under 35 U.S.C. 103(a)

Claims 21, 22 and 23-31 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over WO 92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770). In addition, the claims were rejected over a combination of WO 92/21375 in view of Moormann et al and in view of Drew et al. Applicants respectfully disagree with the Examiner and the following remarks apply to both the rejection based on WO 92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770) and the rejection based on WO

92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770) in view of Drew et al.

The Examiner is relying on the teachings of claim 4 of WO 92/21375 and stating that the vector of that claim "corresponds to the infectious agent, not the sequence disclosed in Wensvoort." Nevertheless, as admitted by the Examiner in the rejection under 35 U.S.C. 102(b) "SEQ ID NO#18 at the 3 prime end of the PRRSV genome **is an inherent feature of the virus of the deposit which is possessed by Wensvoort *et al*."** There is nothing in Wensvvoort that discloses a DNA comprising the full-length sequence including SEQ ID NO: 18. While Wenswoort may generically refer to a vector in claim 4, there is nothing in Wenswoort that shows that such a vector contains an infectious clone, and there is no teaching in Wenswoort on how the skilled person should go about making an infectious clone. Nowhere in Wenswoort is there any teaching that it is possible to for their "vector" of claim 4 to be one that comprises an infectious clone. The Examiner states that "this vector corresponds to the infectious agent". It does not. The only disclosure in Wenswoort of how to create the vector would have to rely on the disclosed sequence or part of the disclosed sequence. That complete sequence is shown in Fig. 1 of the cited reference, and if the skilled individual took that sequence to create a vector as proposed by the Examiner, such an endeavor would not result in an infectious clone because it lacks the 5' terminus represented by SEQ ID NO 18. The Examiner has failed to point to the teaching in Wenswoort that states that the sequence shown in Fig. 1 of the reference is not the complete sequence and that the skilled person should obtain the deposited virus to obtain the remainder of the sequence. There is nothing in the disclosure of the Wensvoort et al reference that suggests that the sequence given therein for the deposited virus is incomplete.

In order to maintain the rejection under 35 U.S.C. 103 the Examiner would have to rely on obviousness based on an inherent feature of a deposited virus. Again, as Applicants have noted, this feature was not known to be important for generating infectious clones until the present invention taught the skilled person to use this feature. Given that there is nothing in either Wensvoort, Moorman et al or Drew et al. that teaches that the utmost 5'end of the WO 92/21375 is essential for production of the an infectious clone, this combination of references cannot render obvious the claimed invention.

To reiterate, the claims as presented are directed to specific **cDNA infectious clones of PRRS virus strain deposited under accession number CNCM I-1102**. As noted in the application, the use of such cDNA clones "circumvent[s] the problems encountered in viral RNA strand synthesis associated with the presence of incomplete viral RNA fragments." [para. 0013]. The specification teaches that "the utmost 5' end of the viral genome in genome length cDNA [creates] an infectious clone" [para. 0068] and that the presence of this 5' cap structure allowed the inventors to overcome the problems of producing the infectious clones.

WO 92/21375 provides the basic disclosure of the nucleic acid sequence of a PRRS virus strain. However, nowhere in WO 92/21375 is there a teaching that it would be desirable to include a specific sequence of SEQ ID NO:18 at the 5' end of the DNA sequence in order to be able to produce an infectious clone that encodes an RNA virus genome to render that clone infectious. Likewise, Moormann et al. fails to provide any guidance as to why a sequence of SEQ ID NO:18 as opposed to any other sequence would be particularly useful in rendering a PRRS virus infectious. Drew et al. does nothing to

supply this additional teaching. Thus, the teachings of the prior art are inadequate for rendering specifically claimed sequences obvious.

While the prior art, including WO 92/21375, may well have identified various PRRS **RNA** viruses and described vectors that contain portions of those viruses there is nothing in that prior art that shows that it is possible to create infectious cDNA clones from those viruses. As specifically noted in the specification, routinely infectious clones (**i.e., DNA clones**) of such viruses were not described (page 10, ¶0029). It was the teachings of the present invention that showed that incorporating a sequence of SEQ ID NO:18 into the utmost 5' end into genome-length cDNA of those viruses to created infectious clones. With this teaching it is now possible to generate infectious isolated **DNA clones** of the PRRS viruses such that the DNA clones may be used to infect non-permissive host cells. As such, these isolated DNA sequences can be used to prepare infectious PRRS viruses in non-permissive cells and can then be used as delivery vehicles for generating an immune response. Wensvoort does not teach making infectious clones from DNA and a simple statement in claim 3 of a "vector" does not provide a teaching that the vector must contain SEQ ID NO:18. In the absence of this express disclosure somewhere in the art the Applicant respectfully submit that neither Drew et al. nor Moormann et al. can be used to render the claims obvious.

Neither of the secondary references show that in order to make an infectious DNA clone of a plus strand RNA virus such the PRRS virus CNCM I-1102 the skilled person would necessarily have to include in the cDNA sequence a sequence of SEQ ID NO:18. In order for the Examiner's "inherent obviousness" argument to work, there must be a teaching in some secondary reference that the sequence of SEQ ID NO:18 was necessary to be part

of the vector disclosed in claim 4 of Wensvoort. It is only by adding this sequence that the present inventors have been able to infect the DNA into a host cell that is not capable of being infected by a wild-type PRRS virus.

Moreover, as described in the present application at Paragraph 004, prior to the present invention the largest infectious clone produced was 12kb in length. Indeed, this is the length of the Pestivirus clone that is the subject of Moormann et al. This is too short a length for a full length PRRS virus genome which is an RNA sequence of about 15kb. In order to make an infectious clone of an RNA virus it is necessary to have a full-lgth reverse transcript that includes the utmost 5' and 3' termini. The 5' terminus of SEQ ID NO:18 was only disclosed for the first time in the present application. The claims of the present invention for the first time describe an infectious DNA molecule which can be used in non-permissive cells to produce infectious PRRS virus clones.

In view of the above discussion and the amendment to the claims, Applicants believe the rejection of claims 21, 22 and 23-31 under 35 U.S.C. 103(a) should be withdrawn.

F. Closing Remarks

Applicants believe the above remarks and amendments overcome the outstanding rejections and Applicants request withdrawal of the rejections and reconsideration of the claims for allowance. No additional fees are believed to be due, however, should fees be deemed necessary or should there be an overpayment, the Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

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